

Tab 1

This License Agreement Must Be
Signed By July 31, 1990. Its
Terms Are Not Available After
July 31, 1990.

COLUMBIA UNIVERSITY

License Agreement
relating to
U.S. Patent No. 4,399,216 et al.

THIS AGREEMENT, dated as of July 31, 1990, between THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK, a New York corporation ("Columbia"), and GENETICS INSTITUTE, INC., a Delaware corporation ("Licensee"),

W I T N E S S E T H:

WHEREAS, research at Columbia concerning the introduction of DNA into eucaryotic cells has resulted in certain useful discoveries that are disclosed and claimed in U.S. Patent No. 4,399,216 and other patents and patent applications owned by Columbia,

WHEREAS, Columbia wishes to license its patent rights in these discoveries to Licensee on a non-exclusive basis for products other than Erythropoietin, and

WHEREAS, Licensee wishes to become licensed under these patent rights;

NOW, THEREFORE, in consideration of the premises and the mutual agreements herein contained, the parties hereby agree as follows:

1. Definitions.

(a) "Affiliate" means any corporation or other business entity that directly or indirectly controls, is controlled by, or is under common control with, Licensee. Control means direct or indirect ownership of, or other beneficial interest in, 50 per cent or more of the voting stock, other voting interest or income of a corporation or other business entity.

(b) "Erythropoietin" means a polypeptide made by the use of genetic engineering techniques which has the biological activity of, and an amino acid sequence substantially the same as that of, naturally-occurring human erythropoietin, the manufacture, use or sale of which polypeptide would, but for the license granted herein, infringe a claim of Licensed Patent Rights in any country

where Licensed Patent Rights exist, regardless of the identity of the country where such manufacture, use or sale occurs.

(c) "Licensed Patent Rights" means U.S. Patent No. 4,399,216, issued August 16, 1983; U.S. Patent No. 4,634,665, issued January 6, 1987; pending U.S. patent application Serial No. 346,089, filed May 2, 1989, a continuation application of U.S. Serial No. 915,273, filed October 3, 1986, now abandoned, which was a divisional application of U.S. Serial 522,408, filed August 11, 1983, now U.S. Patent No. 4,634,665, issued January 6, 1987; which in turn was a divisional application of U.S. Serial No. 124,513, filed February 25, 1980, now U.S. Patent No. 4,399,216, issued August 16, 1983; pending U.S. patent application Serial No. 249,454, filed September 26, 1988, a continuation application of U.S. Serial No. 103,807, filed October 1, 1987, now abandoned, which was a continuation application of U.S. Serial No. 683,251, filed December 17, 1984, now abandoned, which in turn was a continuation application of U.S. Serial No. 358,206, filed March 15, 1982, now abandoned; all corresponding foreign patent applications including European Patent No. 045,809 and all national patents based thereon; any and all divisions, continuations and continuations-in-part based on any of the foregoing; any and all patents issued therefrom and any and all reissues or extensions thereof.

(d)(i) "Licensed Products" means products excluding Erythropoietin, the manufacture, use or sale of which is covered by a claim of Licensed Patent Rights which have neither expired nor been held invalid by a court of competent jurisdiction from which no appeal has or may be taken.

(ii) "End Products" means Licensed Products sold in form for use by an end user and not intended for, or not intended for use in, further chemical transformation, genetic manipulation, processing, formulation, compounding or packaging.

(iii) "Bulk Products" means Licensed Products other than End Products.

(iv) "Basic Genetic Products" means Bulk Products that are sold for use primarily for further genetic manipulation and services sold to another which involve the use of Licensed Patent Rights.

(v) "Process Improvements" means the savings achieved in the cost of manufacturing a Licensed Product relative to the previous cost of manufacturing essentially the same product by a process not covered by a claim of Licensed Patent Rights; cost of manufacturing shall be determined in accordance with generally accepted accounting principles.

(vi) End user for purposes of this paragraph (d)

means a person or entity whose use of a product results in its destruction, loss of activity or loss of value.

(e) "Net Sales" means the total invoice or contract price charged by Licensee and its Affiliates to third parties for the sale of Licensed Products, less returns and customary trade discounts actually taken, outbound freight, value added, sales or use taxes and customs duties. If an End Product is sold in combination with another active component or components, Net Sales for purposes of determining royalties on the combination shall be calculated by multiplying Net Sales of the combination by the fraction $A/(A+B)$, where A is the total invoice price of the End Product if sold separately and B is the total invoice price of any other active component or components in the combination if sold separately. If the End Product and the other active component or components in the combination are not sold separately, Net Sales for purposes of determining royalties on the combination shall be calculated by multiplying Net Sales of the combination by the fraction $C/(C+D)$, where C is the total direct cost of manufacturing the End Product and D is the total direct cost of manufacturing the other active component or components in the combination. Cost of manufacturing for the purposes of this paragraph (e) shall be determined in accordance with generally accepted accounting principles.

2. License Grant.

(a) Columbia hereby grants to Licensee and its Affiliates, subject to the terms and conditions of this Agreement, a non-exclusive, non-transferable license, under Licensed Patent Rights, without the right to grant sublicenses, to make, have made, use and sell Licensed Products.

(b) All rights granted by Columbia under this Agreement are subject to any rights required to be granted to the Government of the United States of America, including without limitation any rights reserved or obligations imposed by the Government pursuant to 35 U.S.C. §200-211, regulations thereunder and the determination letter to Columbia from the Department of Health and Human Services dated February 24, 1981, a copy of which is attached hereto as Appendix A. Licensee will provide all information and assistance necessary to enable Columbia to comply with its obligations to the Government in connection with the subject matter of this Agreement.

(c) Columbia hereby waives, and covenants not to sue Licensee for, any claim of infringement based on Licensee's making, using or selling any Licensed Product prior to the effective date of this Agreement.

3. Fees and Royalties.

(a) Upon the signing of this Agreement, Licensee shall pay Columbia a non-refundable fee of \$210,000, of which Licensee may credit \$30,000 against royalty payments due for 1990.

(b) On the first day of January of each calendar year following 1990, Licensee shall pay Columbia a non-refundable annual fee of \$30,000. In each year, beginning in 1991, in which Licensee owes royalty payments to Columbia, Licensee may credit that year's annual fee against royalty payments due.

(c) All sales by Licensee of Licensed Products, except sales to the United States Government, shall be subject to royalties as provided in Sections 3(d) through 3(g).

(d) Licensee shall pay Columbia a royalty equal to 1.5% of Net Sales of End Products made or sold in a country where Licensed Patent Rights exist.

(e) Licensee shall pay Columbia a royalty equal to 3.0% of Net Sales of Bulk Products made or sold in a country where Licensed Patent Rights exist.

(f) Licensee shall pay Columbia a royalty equal to 12.0% of Net Sales of Basic Genetic Products made or sold in a country where Licensed Patent Rights exist.

(g) Licensee shall pay Columbia a royalty equal to 15.0% of the cost savings achieved each calendar quarter by Process Improvements in countries where Licensed Patent Rights exist.

(h) If Licensee owes royalties under more than one of Sections 3(d), 3 (e), 3 (f) and 3 (g) based on Net Sales of, or Process Improvements with respect to, the same Licensed Product, Licensee shall pay only the highest royalty due under any one paragraph.

(i) If the manufacture, use or sale by Licensee of a Licensed Product in any country where Licensed Patent Rights exist would infringe a patent in that country, which patent is owned by a third party, Licensee shall be entitled to deduct from the royalties due from Licensee to Columbia based upon sales of such Licensed Products in such country certain royalties paid by Licensee to such third party for a license under such patent. Specifically, Licensee may deduct from the royalties due from Licensee to Columbia based upon sales of such Licensed Product in such country up to one-third of the royalties paid by Licensee to such third party based upon such sales, provided such deductions shall not exceed one-third of the amount of royalties due from Licensee to Columbia on such sales.

(j) If Columbia, under substantially identical conditions, grants to a third party a license with respect to Licensed Products under Licensed Patent Rights, having royalty rates more favorable to such third party than those set forth herein, Columbia will give Licensee the benefit of such rates.

4. Reports and Payments.

(a) Within 90 days after the close of each calendar quarter during the term of this Agreement, including the calendar quarter following termination of this Agreement, Licensee shall deliver a report certified by an officer of Licensee to Columbia, in form acceptable to Columbia, of the amount of Net Sales of Licensed Products sold by Licensee and its Affiliates, the amount of any Process Improvements and the amount of royalties due to Columbia under Section 3 of this Agreement. If a payment is due, Licensee shall remit such payment with the report.

(b) Licensee shall make payments in the United States in United States Dollars. All royalties due on Net Sales made in currency other than United States Dollars shall be converted to United States Dollars on the basis of the commercial rate of exchange in effect for such transfers at Chemical Bank in New York, New York, on the last business day of the period for which such royalties were due. If transfer restrictions exist in any country which prevent making payments in the United States, Licensee shall make all reasonable efforts to procure whatever licenses or permits are required to waive such restrictions or otherwise facilitate the making of such payments. If Licensee's efforts fail to permit making payments in the United States, Licensee may make such payments in local currency in the country where such restrictions exist by depositing the payments in a local bank or other depository designated by Columbia. Licensee may deduct or withhold from such payments and pay to the proper taxing authority for Columbia's account any taxes or fees required by law or regulation to be deducted or withheld from such payments. Licensee shall send to Columbia evidence of such payments.

(c) Licensee shall maintain accurate books and records in sufficient detail to enable the payments due hereunder to be determined. Such records shall be available on request by Columbia for inspection, during normal business hours, by Columbia's independent certified public accountant for three years after the calendar year to which they pertain, for purposes of verifying the accuracy of the reports and payments made by Licensee.

5. Term of Agreement.

(a) This Agreement shall be effective as of the date first set forth above and shall continue in full force and effect, unless earlier terminated as herein provided, until the

expiration of the last to expire of the Licensed Patent Rights.

(b) This Agreement and the licenses granted under it may be terminated by Columbia (i) upon 30 days' written notice to Licensee for Licensee's material breach of this Agreement if Licensee has failed to cure its breach within 30 days after written notice thereof given by Columbia or (ii) if Licensee commits any act of bankruptcy, become insolvent, files a petition under any bankruptcy or insolvency act or has any such petition filed against it because of the happening of such act or event. Without limiting the generality of the foregoing, Licensee shall be in material breach of this Agreement if it fails to make all reports or pay all fees and royalties when due.

(c) Licensee may terminate this Agreement at any time upon twelve months' written notice to Columbia.

(d) Upon any termination of this Agreement for any reason other than Licensee's failure to cure a material breach of this Agreement, Licensee shall have the right, for one year or such longer period as the parties may reasonably agree, to dispose of Licensed Products or substantially completed Licensed Products then on hand, and to complete orders for Licensed Products then on hand, and royalties shall be paid to Columbia with respect to such Licensed Products as though this Agreement had not terminated.

(e) Termination of this Agreement shall not terminate Licensee's obligations to pay fees and royalties that shall have accrued hereunder or Licensee's obligations under Sections 4, 7 and 8 of this Agreement.

6. Warranty. Nothing in this Agreement shall be construed as a warranty or representation by Columbia as to the validity of any Licensed Patent Rights. Nothing in this Agreement shall be construed as a warranty or representation by Columbia that anything made, used, sold or otherwise disposed of under any license granted under this Agreement is, or will be, free from infringement of domestic or foreign patents of third parties.

7. Prohibition Against Use of Name. Neither Licensee nor any of its Affiliates will use the name, insignia or symbols of Columbia, its faculties or departments, or any variation or combination thereof, or of the name of any trustee, faculty member, other employee or student of Columbia for any purpose whatsoever without Columbia's prior written consent.

8. Indemnity. Licensee will indemnify and hold Columbia harmless against all actions, suits, claims, demands, or prosecutions that may be brought or instituted against Columbia based on or arising out of this Agreement, including, without limitation, the following:

(a) the manufacture, packaging, use or sale of Licensed products by Licensee, any Affiliate or their transferees;

(b) any representation made or warranty given by Licensee or any Affiliate with respect to any Licensed Product; and

(c) the use by Licensee or any Affiliate of any process under Licensed Patent Rights.

9. Notices. Any notice, report, payment or statement required or permitted under this Agreement shall be sufficient if sent by certified mail (return receipt requested), postage prepaid,

if to Columbia, to:

Director
Office of Science and
Technology Development
Columbia University
411 Low Memorial Library
New York, New York 10027

copy to:

General Counsel
Columbia University
110 Low Memorial Library
New York, New York 10027

if to Licensee, to:

Genetics Institute, Inc.
87 Cambridge Park Drive
Cambridge, Mass. 02140
Attention: Bruce C. Eisen, Esq.

or to such other address as a party may specify by notice hereunder.

10. Miscellaneous. This Agreement shall be governed by New York law applicable to agreements made and to be performed in New York.

This Agreement is not assignable except by the Licensee (i) upon the sale or transfer of all or substantially all of its business or assets relating to its operations exercising the licenses granted hereunder, or (ii) to any Affiliate of Licensee, provided that, in the event of such assignment, the term Licensee as used in this Agreement shall mean such Affiliate, and provided further the original Licensee shall remain liable for the performance of such Affiliate.

This Agreement may be amended only by an instrument in writing duly executed on behalf of the parties.

IN WITNESS WHEREOF, Columbia and Licensee have caused this Agreement to be executed by their duly authorized representatives as of the date first set forth above.

THE TRUSTEES OF COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK

By Jack M. Granoff
Name: JACK M. GRANOFF
Title: DIRECTOR, OFFICE OF SCIENCE
AND TECHNOLOGY DEVELOPMENT

GENETICS INSTITUTE, INC.

By Bruce M. Eisen
Name:
Title: V.P. - Chief Patents Counsel